REMARKS

Reconsideration of the above-identified application is respectfully requested.

Claims 1, 2, and 4–13 remain in the application. Claims 3 and 14–19 have been cancelled. Claim 1 has been amended to describe the composition as non-hygroscopic. Support for this term is found throughout the specification. The term "additional" has been added to modify organic acids to distinguish the stabilizer from the therapeutic agent. This amendment is being made in view of the Examiner's comments. It is evident throughout the specification that the organic acids used as stabilizers are organic acids used in additional to the therapeutic agent.

Section 112 Rejection

Claim 1 has be rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claim 1 incorporated the phrase "second acid source," which the Examiner cannot find in the specification and is therefore rejecting the phrase as being new matter. The phrase "single acid source" has been deleted from claim 1, and therefore, the rejection should be withdrawn.

Section 103 Rejections

Claims 1, 2, and 4–13 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Anzaghi, International Pat. Pub. No. WO 02/39992, in view of Strom, U.S. Pat. No. 7,250,176.

The Anzaghi reference teaches adducts of polysaccharide polymers with quinolonic antibacterial agents as the active ingredients. The quinolonic antibacterial agents are between 40% and 80% by weight of the total adduct. The adducts can be administered both orally and parentally. Among the natural polysaccharide polymers, dextrins are preferred, as well as inulin, and for oral preparations, maltodextrins. The natural polysaccharides are biocompatible and

inert. The quinolone and polysaccharide are able to interact without forming covalent and ionic bonds.

One skilled in the art would not choose the teachings of the Anzaghi reference for assistance because of the requirement for an adduct formed with a polysaccharide polymer, which is not disclosed in the claimed invention. In addition, the Anzaghi reference does not disclose an acid stabilizer, which is required in Applicants' claimed invention.

The Strom reference does not contain any teaching or suggestion for combination with the Anzaghi reference. The Strom reference discloses a dosage form of amoxicillin that contains copious amounts of the therapeutic agent. Amoxicillin has different pharmacokinetic, chemical, and physical properties from quinolonic antibacterial agents. It is unlikely that one skilled in the art would be studying formulations of amoxicillin in an effort to create non-hygroscopic formulations of quinolonic antibacterial agents prepared by wet granulation. Amoxicillin is highly soluble in water. The amoxicillin formulation is contained in a bilayer tablet, a first portion having an immediate-release phase and a second portion having a slow-release phase. In col. 14, ll. 43–53, the Strom reference discloses use of an organic acid as a release-retarding excipient. This is used in the slow-release phase of the bilayer tablet and is present in a molar ratio of amoxicillin to citric acid ranging from 100:1 to 1: 10, preferably 50:1 to 1:5, more preferably 20:1 to 1:2, and even more preferably 1:1, especially in the slow-release layer of the tablet. The suggestion that a bilayer tablet having quick-release and slow-release formulations of amoxicillin, with citric acid used a release-retarding excipient, would not lead one skilled in the art to use of citric acid or other claimed organic acids as stabilizers in a non-hygroscopic composition containing quinolonic antibacterial agents in a stabilizer. The combination of an adduct containing polysaccharide polymers and a quinolonic antibiotic with a formulation

containing amoxicillin and many other diverse ingredients with citric acid serving as a release-retarding agent in a slow-release portion of a bilayer tablet would not lead one skilled in the art to the claimed invention. Amoxicillin is highly water soluble, and one skilled in the art would not study formulations of amoxicillin to gain knowledge about non-hygroscopic compositions for use in preparing a tablet by wet granulation containing quinolonic antibacterial agents and an inorganic or organic acid stabilizer. The amoxicillin formulation would hydrate readily, therefore obviating itself as means for creating a non-hygroscopic composition containing quinolonic antibiotics. Further, the amounts of citric acid used in the Strom reference are based on molar amounts. Example 5 discloses an amoxicillin formulation having 8.3% by weight of citric acid, which is outside the claimed range of stabilizer.

Claims 1, 2, and 4–13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the Katdare reference, U.S. Pat. No. 4,639,458, in view of the Strom reference.

The Katdare reference describes direct compression tablet formulation containing norfloxacin. The specification describes that processing aids may be utilized, including, for example, a disintegrant, a filler/binder, and lubricant, with a colorant being optionally added. The tablet may be film coated. In the list of processing aids, neither a stabilizer nor an organic or inorganic acid is disclosed. Therefore, the reference does not motivate one to use a stabilizing agent, much less a stabilizing agent comprising an inorganic acid or organic acid as claimed in the present invention.

The Office Action states that the teachings of the Strom reference may be added to the Katdare reference to arrive at Applicants' claimed invention. As stated above, the Strom reference discloses high dosages of amoxicillin in a bilayer tablet so that the amoxicillin may be released immediately and in a slow-release regimen. The Strom reference also identifies

anhydrous citric acid as a release-retarding agent/excipient. However, the Strom reference does not teach the claimed percentages, nor does it teach that the release-retarding agent/excipient is a stabilizer. Applicants do not disclose a bilayer tablet nor does Katdare. Nevertheless, the Examiner believes that the teachings of the two references can be combined so that the Katdare reference using direct compression to form tablets may include anhydrous citric acid to create a finished composition. However, Applicants do not claim a slow-release composition nor does Katdare describe one. Indeed, in the comparative examples, the Katdare reference shown in cols. 2 and 3 is compared to a prior art Italian formulation for breaking strength and dissolution percent at 10, 20, and 30 minutes. Both formulations have similar faults. In reviewing the data, it can be seen that the Katdare reference is not describing a slow-release formulation. It would be highly unusual for one skilled in the art to take the teachings of the Strom reference, which describes a slow-release composition using anhydrous citric acid, to combine with the Katdare reference in a process for making a norfloxacin composition by direct compression. Only by reviewing Applicants' invention and using hindsight analysis would one skilled in the art venture to do this. This type of analysis is improper.

There is another major difference between the teachings of the Strom reference and the Anzaghi and Katdare references that was briefly mentioned above. The Strom reference teaches various compositions for preparing a bilayer tablet for releasing amoxicillin. According to the *Merck Index, 12th ed.*, p. 619, amoxicillin has a water solubility (mg/ml) of 4.0. In preparing an amoxicillin composition, care must be taken so that hydration does not occur. It would be highly unusual for a substance having a 4.0 solubility to be made into a non-hygroscopic composition, which is prepared via wet granulation as claimed by Applicants. Using the same water solubility parameters for norfloxacin at 25°C, the water solubility is 0.28. Preparing a non-hygroscopic

composition or even using a wet granulation method is more efficient with norfloxacin than with amoxicillin. One skilled in the art would hardly take the teachings from a composition comprising a bilayer tablet having two different release rates for a water-soluble antibiotic and use them to produce a non-hygroscopic composition, such as one claimed by Applicant. Indeed, the disclosure of the Strom reference teaches away from the teachings of the Anzaghi and Katdare references. Therefore, the references, taken singly or in combination, do not render the claimed invention obvious.

Conclusion

The claims meet the requirements of 35 U.S.C. §§ 112 and 103. Therefore, an early Notice of Allowance of the above-identified application is respectfully requested. The Examiner is invited to contact Applicants' representative if questions arise.

Respectfully submitted,

VEDDER PRICE P.C.

Date: October 17, 2008

By: _____
W. Dennis Drehkoff, Reg. No. 27,193

222 N. LaSalle St., Suite 2600
Chicago, Illinois 60601
phone: (312) 609-7707
fax: (312) 609-5005